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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/003,496	11/01/2001	Torben Laesgaard Nissen	0218us210	7340
30560	7590	09/17/2004	EXAMINER	
MAXYGEN, INC. INTELLECTUAL PROPERTY DEPARTMENT 515 GALVESTON DRIVE RED WOOD CITY, CA 94063			MERTZ, PREMA MARIA	
			ART UNIT	PAPER NUMBER
			1646	

DATE MAILED: 09/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/003,496

Applicant(s)

NISSEN ET AL.

Examiner

Prema M Mertz

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 August 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6, 8, 9, 22-27 and 34 is/are pending in the application.
- 4a) Of the above claim(s) 34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6, 8-9, 22-27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. Claims 7, 10-21, 28-33 have been canceled on 8/18/2004. New claim 34 has been added on 8/18/2004. Claims 2-3, and amended claims 1, 4, 5-6, 8-9, 22-27 (8/18/04) are under consideration.

Applicants request rejoinder of the subject matter of claim 34 (see In re Ochiai (37 USPQ2d 1127 (Fed. Cir. 1995)), in which a new, unobvious material is used in a known process. Ochiai determined that a process was free of the prior art if it employed a product which was free of the prior art. However, only if the product claims 1-6, 8-9, 22-27 are found allowable, the subject matter of the product claims will be rejoined with process claim 34, if the process claim is of the same scope as the allowable product claims.

2. Receipt of applicant's arguments and amendments filed on 8/18/04 is acknowledged.

3. The following previous rejections and objections are withdrawn in light of applicants amendments filed on 8/18/2004:

- (i) the objection to the title of the invention;
- (ii) the rejection of claims 1-6, 8-11, 14-17, 20-27 and 29-32 under 35 U.S.C. § 112, first paragraph;
- (iii) the rejection of claims 1-27, 29-33 under 35 U.S.C. § 112, second paragraph.

4. Applicant's arguments filed on 8/18/2004 have been fully considered but were persuasive in part. The issues remaining are stated below.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

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6. Claims 1-6, 8-9, 22-27 are rejected under 35 U.S.C. § 103 as being unpatentable over Ishikawa et al (US Patent No. 5,824,778) in view of Sytkowski (WO 99/38891).

This rejection is maintained for reasons of record set forth at pages 8-9 of the previous Office action (3/18/2004).

Applicants argue that the Sytkowski reference actually teaches away from PEGylation as a means for increasing the biological activity of proteins and have cited pages 1-2 of the reference. However, contrary to Applicants arguments, the primary reference by Ishikawa teaches in column 8, Table 2 that PEGylation increases the biological activity in monomeric hG-CSF and in column 9, lines 6-10 and in Table 3, that PEG bound to G-CSF increased the activity of G-CSF. The instant claims do not recite that biological activity is increased. Furthermore, the Ishikawa reference clearly demonstrates that the biological activity increases in monomeric hG-CSF molecules coupled to PEG i.e. in spite on binding to PEG, the hG-CSF had increased activity. Therefore, dimeric or multimeric forms of hG-CSF-PEG will also be expected to have an increased activity shown by monomeric hG-CSF-PEG since as evident from Ishikawa, PEG does not couple to hG-CSF at the active site of the hG-CSF. If PEG had bound to the active site of hG-CSF protein, the protein molecule would have lost its biological activity. The Sytkowski reference does not teach away from obtaining multimers of hG-CSF bound to PEG. Even assuming it does teach away, the primary reference by Ishikawa teaches that hG-CSF biological activity was enhanced by PEG coupling.

Applicants are incorrect in their arguments that one skilled in the art would not be motivated to combine the teachings of Ishikawa et al and Sytkowski since Ishikawa is silent on the concept of mutimerization and Sytkowski teaches away from the combination of

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multimerization and PEGylation. If the primary reference by Ishikawa taught all the limitations of the claims (i.e. the multimerization), this rejection would be a 35 U.S.C. § 102(b) rejection rather than a 35 U.S.C. § 103 rejection. PEG is coupled to a protein to increase the protein's circulating half-life. Ishikawa has clearly demonstrated in column 8, Table 2 and column 9, Table 3, that PEG linked to hG-CSF increases the biological activity of hG-CSF. Irrespective of the length of the hG-CSF, i.e. monomers, dimers or trimers, PEG binding to hG-CSF, from the teachings of Ishikawa alone, would be expected to increase the biological activity of hG-CSF monomers, dimers or trimers because PEG coupling to the hG-CSF protein is not at the active site of the hG-CSF. Therefore, it would have been obvious to one having ordinary skill in the art to modify the hG-CSF polypeptide of Ishikawa et al. such that it includes the multimers of the monomeric hG-CSF polypeptide bonded to PEG to obtain a multimeric hG-CSF protein with an increased circulating half-life, as taught by Sytkowski, to obtain the known functions and advantages of hG-CSF as per the teachings of Ishikawa. It would be obvious to obtain multimers of the hG-CSF protein conjugated to PEG, to improve the therapeutic potential of hG-CSF. One would have been motivated to obtain multimers comprising hG-CSF and PEG to decrease its clearance rate in vivo and also since the multimer protein would have greater biological activity than the same amount of hG-CSF alone.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (571) 272-0961.

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prema Mertz
Prema Mertz Ph.D.
Primary Examiner
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September 14, 2004